Amendment to the Claims:

1.-21. (Canceled)

22. (Original) A method of screening for substances which are capable of inhibiting the phosphorylation of a tau protein by casein kinase 1 (CK1), wherein the tau protein comprises one or more phosphorylation sites, the method comprising:

(a) contacting at least one candidate substance, the tau protein and casein kinase 1 under conditions in which the casein kinase 1 is capable of phosphorylating the site(s) of the tau protein in the absence of the candidate substance;

(b) determining whether, and optionally the extent to which, the candidate substance inhibits the phosphorylation of the tau protein at one or more sites of the tau protein by casein kinase 1; and,

(c) selecting the candidate substance which inhibits phosphorylation of the tau protein at one or more of the sites.

23. (Original) The method of claim 22, wherein the casein kinase 1 is a fragment or derivative of full length casein kinase 1 having the amino acid sequence set out between amino acids 1 and 428 inclusive in SEQ ID NO: 1.

24. (Currently amended) The method of claim 22~~ or claim 23~~, wherein the casein kinase 1 has greater than 80% sequence

identity with full length casein kinase 1 having the amino acid sequence set out between amino acids 1 and 428 inclusive of SEQ ID NO: 1.

25. (Currently amended) The method of claim 22 ~~or claim 23~~, wherein the nucleic acid molecule encoding the casein kinase 1 is capable of hybridising under stringent conditions to a nucleic acid molecule encoding full length casein kinase 1 having the amino acid sequence set out in SEQ ID NO: 1.

26. (Currently amended) The method of ~~any one of claims 21 to 25~~claim 22, wherein the tau protein is paired helical filament tau.

27. (Currently amended) The method of ~~any one of claims 21 to 24~~claim 22, wherein the tau protein is a fragment or derivative of full length tau protein having the amino acid sequence set out between amino acids 1 and 441 inclusive in SEQ ID NO: ~~3~~2.

28. (Currently amended) The method of ~~any one of claims 21 to 27~~claim 22, wherein the tau protein has greater than 80% sequence identity with full tau protein having the amino acid sequence set out between amino acids 1 and 441 inclusive in SEQ ID NO: ~~3~~2.

29. (Currently amended) The method of ~~any one of claims 21 to 28~~claim 22, wherein a nucleic acid molecule encoding the tau protein is capable of hybridising under stringent conditions to a nucleic acid molecule encoding full length tau protein having the amino acid sequence set out in SEQ ID NO: 3.

30. (Currently amended) The method of ~~any one of claims 21 to 29~~claim 22, wherein the casein kinase 1 phosphorylates tau protein at one or more sites selected from the group consisting of (S46/T50), S113, S131, T149, T169, S184, S208, (S210/T212), S214, S237, S238, S241, S258, S262, T263, S285, S289, S305, S341, S352, S356, T361, T373, T386, (S412/S413/T414), S416, S433 and S435 of tau protein.

31. (Original) The method of claim 30, wherein the sites of the tau protein are selected from S262 and/or S356.

32. (Original) The method of claim 30, wherein the sites of the tau protein at one or more sites selected from the group consisting of S113, S258, S289, S416, S433 and S435.

33. (Currently amended) The method of ~~any one of claims 21 to 32~~claim 22, wherein the method comprises determining the effect of contacting the candidate substance(s) with a combination of kinases, simultaneously or sequentially applied to the candidate substances and casein kinase 1.

34. (Original) The method of claim 33, wherein the combination of kinases comprises casein kinase 1 (CK1) in combination with one or more of casein kinase 2 (CK2), protein kinase A (PKA), glycogen synthase kinase 3α (GSK-3α) or glycogen synthase kinase 3β (GSK-3β).

35. (Original) The method of claim 33, wherein the combination of kinases comprises casein kinase 1 (CK1) in combination with PKA and GSK-3β.

36. (Currently amended) The method of ~~any one of claims 21 to 35~~claim 22, wherein the method comprises determining in step (b) whether, and optionally the extent to which, the candidate substance inhibits the phosphorylation of a substrate by the casein kinase 1.

37. (Currently amended) The method of claim 36, wherein the substrate of casein kinase 1 is ~~not~~other than a tau protein or a fragment thereof.

38. (Currently amended) The method of claim 36~~ or claim 37~~, wherein the method further comprises confirming whether a candidate substance selected in an initial screen has the property of inhibiting the phosphorylation of the tau protein under conditions in which the casein kinase 1 is capable of

phosphorylating the site(s) of the tau protein in the absence of the candidate substance.

39. (Currerntly amended) The method of ~~any one of claims 21 to 38~~claim 22, wherein the step of determining the presence, absence or extent of phosphorylation at one or more sites of the tau protein employs mass spectroscopy or a site specific recognition agent which is capable of distinguishing between a phosphorylated and a non-phosphorylated site.

40. (Original) The method of claim 39, wherein the site specific recognition agent is a monoclonal antibody.

41. (Currently amended) The method of ~~any one of claims 21 to 40~~claim 22, wherein the screening is carried out in a multiplex assay employing a solid phase on which a plurality of substrates are immobilised.

42. (Original) The method of claim 41, wherein the substrates correspond to phosphorylation sites of tau protein.

43. (Currently amended) The method of ~~any one of claims 21 to 42~~claim 22, ~~the method~~ comprising ~~having identified a candidate substance as an inhibitor of casein kinase 1,~~ the further step of optimising the structure of the selected candidate substance.

44. (Currently amended) ~~A~~The method of claim 22 which comprises at least one of ~~having identified a candidate substance by the method of any one of claims 21 to 43,~~ the further steps of manufacturing the selected candidate substance ~~and/or~~and formulating it the selected candidate substance in a pharmaceutical composition.

45. (Currently amended) A method of preparing a pharmaceutical composition or medicament, the method comprising:

(i) identifying a casein kinase 1 inhibitor according to ~~any one of claims 1 to 43~~claim 22;

(ii) optimising the structure of the casein kinase 1 inhibitor; and

(iii) preparing the pharmaceutical composition or medicament containing the optimised casein kinase 1 inhibitor.

46. (Currently amended) A substance ~~obtainable~~obtained by the method of ~~any one of claims 1 to 43~~claim 22.

47.-49. (Canceled)

~~48.~~50. (Currently amended) A method of screening for substances which are capable of inhibiting the phosphorylation of a tau protein at a phosphorylation site at position Y394 by fyn, the method comprising:

(a) contacting at least one candidate substance, the tau protein and fyn under conditions in which the fyn is capable of phosphorylating position Y394 of the tau protein in the absence of the candidate substance;

(b) determining whether, and optionally the extent to which, the candidate substance inhibits the phosphorylation of the tau protein at position Y394 of the tau protein by fyn; and,

(c) selecting the candidate substance which inhibits phosphorylation of the tau protein at position Y394.

~~49.~~51. (Currently amended) A method of screening for substances which are capable of inhibiting phosphorylation by a kinase at least one ~~or more of the site(s)~~site of a tau protein selected from the group consisting of S68, T69, T71, (T111/S113), S191, S258, S289, (T414/S416), T427, S433, S435 and Y394, the method comprising:

(a) contacting at least one candidate substance, a tau protein which comprises said at least one ~~or more of the~~ phosphorylation site~~s~~ and a kinase which is capable of phosphorylating the tau protein under conditions in which the kinase is capable of phosphorylating one or more of the sites of the tau protein in the absence of the candidate substance;

(b) determining whether, and optionally the extent to which, the candidate substance inhibits the phosphorylation of the tau protein at one or more sites of the tau protein; and,

(c) selecting the candidate substance which inhibits phosphorylation of the tau protein at one or more of the sites.

~~50.~~52. (Currently amended) A method of screening for substances which are capable of promoting dephosphorylation of a tau protein by a phosphatase at one or more of the site(s) of a tau protein selected from the group consisting of S68, T69, T71, (T111/S113), S191, S258, S289, (T414/S416), T427, S433, S435 and Y394, the method comprising:

(a) contacting at least one candidate substance, a tau protein comprising one ~~or more the~~at least phosphorylation site and a phosphatase which is capable of dephosphorylating the tau protein under conditions in which the phosphatase is capable of dephosphorylating the site(s) of the tau protein in the absence of the candidate substance;

(b) determining whether, and optionally the extent to which, the candidate substance promotes the dephosphorylation of the tau protein at one or more sites of the tau protein; and,

(c) selecting the candidate substance which promotes dephosphorylation of the tau protein at one or more of the sites.

53. (New) A method for the treatment of a tauopathy in a patient in need of said treatment, said method comprising

administering to said patient a substance obtained by the method of claim 22.

54. (New) The method of claim 51 wherein the tauopathy is Alzheimer's disease, frontotemporal dementia with Parkinsonism linked to chromosome 17 (FTDP-17), progressive supranuclear palsy (PSP), Pick's disease, corticobasal degeneration, multisystem atrophy (MSA), neurobasal degeneration with iron accumulation, type 1 (Hallervorden-Spatz), argyrophilic grain dementia, Down's syndrome, diffuse neurofibrillary tangles with calcification, dementia pugilistica, Gerstmann-Sträussler-Scheinker disease, myotonic dystrophy, Niemann-Pick disease type C, progressive subcortical gliosis, prion protein cerebral amyloid angiopathy, tangle only dementia, postencephalitic parkinsonism, subacute sclerosing panencephalitis, Creutzfeldt-Jakob disease, amyotrophic lateral sclerosis/parkinsonism-dementia complex, non-Guamanian motor neuron disease with neurofibrillary tangles/dementia, and Parkinson's disease.